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**EDITORIAL****Beyond traditional CBRN force protection – a future of CBRN hardened super-soldiers?**David J Heslop<sup>a</sup><sup>a</sup>School of Public Health and Community Medicine, Faculty of Medicine, University of New South Wales, Kensington, NSW, 2052, Australia

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**Abstract**

Current momentum in military research efforts has opened the possibility for the enhancement, but also augmentation of military personnel for the purpose of achieving advantage over rivals. Rapid technological advances are currently breaking ground well ahead of prudent commentary and consideration of impacts on human society, ethics, geopolitics and military operations. This has potentially allowed friend and foe alike to exploit opportunities to develop completely novel countermeasures and defences and develop new threats in Chemical, Biological, Radiological and Nuclear (CBRN) military operations. In this editorial, two recent technological developments driving medical countermeasure research are highlighted as examples. How such developments impact on capability competitions – in other words, driving new arms races – in near-peer rivals is discussed. The profound potential impacts of these new technologies on the fundamentals of human existence as we understand it today are highlighted.

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**Introduction**

One vision of future conflict involves the use of medical, pharmaceutical and force protection technologies that enhance, support or improve physiological resilience, combat capabilities and characteristics of a soldier, allowing them to survive and function effectively despite significant Chemical, Biological or Radiological and Nuclear (CBRN) exposures that would normally cause serious injury or death. Enhancements to physiological and physical characteristics of personnel are risk controls commonly employed to improve health resilience, combat survivability and increase command assurance that personnel are best prepared to undertake operations (1). Simple examples of enhancement in use in training exercises and military operations today are physical conditioning, acclimatisation, malaria prophylaxis and travel vaccination (1-3). As military offensive technology has developed over centuries there has been a matched development of defensive and medical technologies driven by military necessity – a medical technology arms race frequently rendering offensive and defensive technologies obsolete. Medical technologies that allow for enhancement of individual physiological and physical resilience have emerged repeatedly since antiquity and continue to be the prime focus of military medical research. Classic examples of such wartime medical innovations are the French introduction of the field military surgeon and triage systems in the Napoleonic wars to improve combat trauma outcomes, the English use of lemon juice for naval and other forces to prevent

Vitamin C deficiency (scurvy), the development of penicillin in the Second World War to prevent infection, and the development of tetanus vaccine to prevent complications of contaminated traumatic wounds (1).

Injured and ill soldiers on the battlefield, enemy or ally, significantly constrain military operations. For example, the logistic burden of casualty management has been extensively documented in all major theatres of war, famously in North-Eastern France in the First World War (4), but also as recently as the first and second Gulf Wars. Similarly, the impact of influenza on the effectiveness and combat power on the German forces on the Western Front in the First World War is a good example of the operational impact caused by infectious disease (5).

Recent technical and scientific developments have opened the door to the enhancement to the innate defences of personnel and reducing the risk of direct harm when operating in CBRN environments. In this article two recent significant CBRN medical countermeasure (MCM) developments will be outlined, followed by a discussion of the benefits and pitfalls associated with the apparent steady technological progression from simple enhancement<sup>1</sup> of innate human characteristics, towards a future of augmentation<sup>2</sup> of physical and physiological characteristics over and above natural capacity and ability – made possible through advances in bionics, robotics, nanotechnology, genetics, miniaturisation, and wireless networking and communications.

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<sup>1</sup> Enhancement is defined here as any improvement to a soldier or soldier system that assists or provides advantage with completing the mission, and is generally temporary or reversible in nature and of minimal harm to the recipient.

<sup>2</sup> Augmentation is defined here as more intensive improvements to the physical, physiological and soldier systems integration for an individual, utilising methods that may be invasive, intensive, permanent or potentially cause longer term or unknown ramifications, or which are not removable or reversible.

## **CBRN Force Protection strongly intersects with Operational Capability**

The current approaches to CBRN systematic risk management in military organisations derive from the well accepted model first published in 1981 by Kaplan and Garrick, and later adopted in various forms in civilian and military organisations around the world (6-11). Operational environments with real CBRN hazards and risks fall at the extreme end of the risk spectrum. Of the numerous risk controls employed to allow personnel to operate safely in a CBRN operational environment, medical countermeasures (MCM) form a major component (4, 5, 12). The proliferation of CBRN agents during the 20<sup>th</sup> Century was matched with a parallel impetus to discover, develop and field effective tactics, techniques and procedures alongside MCM to protect soldiers against those agents and protect operational effectiveness. Countermeasures were either discovered by serendipitous flash of insight, overt and covert information transfer from enemy to allies<sup>3</sup>, battlefield innovation in the face of extreme suffering, and most commonly by the laborious and systematic search for novel compounds by research conducted in key research organisations (4, 5, 12).

Over history, the development of new MCMs subsequently allowed commanders to actively consider undertaking operations previously seen as risky or failure prone (4, 5). At the operational level, MCM allow planners to extend lines of communication and decrease the requirement to allocate maximum medical logistics as casualties are simply prevented and the burden avoided entirely. At a tactical level, the utilisation and availability of MCMs increases the confidence and morale of combat personnel, and facilitates and enhances leadership in a highly challenging combat environment.

It has been widely recognised that the absence of MCM constrains operational planning, limits freedom of manoeuvre and flexibility, and can easily result in premature culmination of a military force, rapid degradation of unit strength on attack with low level exposures, and denial of the possibility of force recovery and reconstitution. In short, the absence of MCM in a CBRN operational environment can readily destroy (not neutralise or degrade as is normally the case in conventional conflict) friendly units. The pathways to a lack of available and adequate MCMs are often failures of intelligence and threat appreciation, inadequate investment in MCM research and development, production failure, direct enemy action and sabotage, and logistic constraints.

Taken together, any inequality in MCM resources between opposing forces in a CBRN environment is likely to rapidly become operationally and strategically decisive. MCM are a critical potential vulnerability in CBRN operations, and their availability must be ensured and protected at all costs. In sum, the intensiveness and effectiveness of CBRN Force Protection has a direct

positive relationship with the balance of operational capability in opposing forces.

For the remainder of this editorial, I will highlight two recent developments in CBRN Force Protection that have implications for the balance of capabilities in opposing military forces and have been recently the subject of intensive research and operational interest.

### **Enhancing innate resilience of soldiers to nerve agents and organophosphates**

Nerve agents are some of the most toxic substances known to man. Weight-for-weight, their toxicity is only surpassed by certain biological toxins such as botulinum neurotoxin. Of the traditional nerve agents (G-series and VX), VX is considered to be the most toxic having a LD<sub>50</sub> in humans of 6-10 mg for skin exposure – equivalent to a drop 2-3mm in diameter (13). Variants of traditional nerve agents have been developed, despite rigorous international prohibitions, having significantly greater toxicity and unique physicochemical characteristics compared to the traditional nerve agents. Nerve agents exert their toxic effect through the inactivation of the enzyme acetylcholinesterase. Acetylcholinesterase acts to limit the amount of acetylcholine present at the synapses between nerves and muscles throughout the nervous system and body. The widespread inactivation of acetylcholinesterase by nerve agent causes generalised muscular and secretory gland dysfunction. The sum total of these effects causes the familiar clinical signs and symptoms of nerve agent intoxication – massive airway secretions, paralysis, respiratory failure and seizures, which are fatal if untreated (13).

Despite the overwhelming toxicity of nerve agents, the human body possesses the ability to cope with certain amount of exposure prior to toxicity. One of the most important elements of the innate system that detoxifies chemical agents in the human body is the butyrylcholinesterase (BuChE) system present most significantly in the serum of circulating blood (14-16). The normal function of the BuChE system is to degrade choline based esters which would otherwise have negative toxic effects in the body. Choline based esters are similar to nerve agents in terms of their biological effects, but are lower in toxicity and are a common hazard in the diets of any herbivorous or omnivorous animals, including humans (15, 17). Common examples of these compounds acting as dietary chemical hazards are the metabolic breakdown products of the anticholinesterase glycoalkaloids solanine, cachenine and solanidine found in the skin of old green potatoes, hormones involved in normal plant development and present in high concentration in some plants, toxic beans such as the calabar bean (the source of physostigmine<sup>4</sup>), and opiates (heroin, opium) and other psychoactive compounds (cocaine) derived from plants. It is hypothesised that the BuChE detoxification system has been conserved through evolution as it confers a survival advantage for species who rely on the intake of botanicals

<sup>3</sup> Or vice-versa

<sup>4</sup> An anticholinesterase pharmaceutical used in anaesthesia and an effective nerve agent simulant

containing anticholinesterase compounds as a normal part of their diet (17).

It has been observed that certain individuals have higher than normal activity of BuChE naturally. This is believed to be due to genetic variation in the BuChE gene encoding the enzyme which results in circulating BuChE having a significantly increased level of general detoxification capacity. These individuals are naturally resistant to high levels of many anticholinergic chemicals found in foods and some pharmaceuticals. Animals which similar mutations have equally been shown to be able to survive nerve agent challenges that are universally lethal to non-mutated animal (14, 16, 18-21), up to 6 times the LD<sub>50</sub> without any symptoms. Human populations possessing similar mutations are thought to be naturally resistant to a wide range of chemical insults, including organophosphates and, almost certainly, nerve agents.

These findings led to the hypothesis that BuChE might be developed as an effective nerve agent MCM that would confer a similar protective effect against nerve agent exposure in the average human – effectively conferring a super-detoxification ability to the recipient. This hypothesis is supported by extensive research and clinical trials undertaken to develop a operationalised MCM (14, 16, 18, 19, 21-31). The human BuChE gene has also recently been incorporated into a bacterial host, for the purpose of large scale production of therapeutic BuChE. It is envisaged that BuChE for field use is administered as a single dose intravenous infusion providing enhanced detoxification coverage for at least 3 days and likely up to 7, after which time the additional BuChE is degraded and the recipients blood profile returns to pre-injection norms (22). One future possibility, now enabled by precision gene editing technologies such as CRISPR-Cas9 and similar constructs, is that additional BuChE genes may be incorporated into the genome of individuals. These genetically modified individuals would be then possess superior detoxification capacity to both nerve agents, organophosphate compounds and many other chemicals and toxicants but with the advantage of not requiring exogenous administration.

### **Enhancing innate resilience to high dose radiation exposure**

Today there exist a number of available technologies that reliably and safely increase the ability of individuals to withstand, without short term negative effect, high dose whole body exposure to radiation. Such exposure could occur in the context of the widespread dissemination of radioisotopes during various military and humanitarian assistance operations, but equally could occur in precision strikes against high profile individuals or capabilities. In either case, high dose radiation exposure is a possible, but invisible and difficult to defend against threat. Acute radiation syndrome occurs in most individuals after they are

exposed to a whole body dose of 1 Gray. Below an exposure of 1 Gray, no obvious clinical symptoms and signs are seen in most individuals, but detectable changes white cell count are seen (32). Between 1 and 10 Gray, the characteristic symptoms and signs of the haemopoietic syndrome predominate. This is characterised by a progressive depletion of white cells in the blood due to the lethal effect of radiation on sensitive progenitor stem cells in the bone marrow. Exposure at this level is generally without physical manifestations after a short initial prodromal period characterised by vomiting and general debility. Above a dose of 10 Gray the gastrointestinal syndrome becomes prominent, followed by a neurological and cardiovascular syndrome at doses between 20 and 50 Gray. Individuals who develop the gastrointestinal, neurological or cardiovascular syndrome have almost always been exposed to radiation doses that are unsurvivable over the course of days to weeks (33).

White blood cells are the circulating component of the body's immune system, and their gradual depletion over approximately 30 days post exposure is responsible for the life-threatening consequences of radiation exposure. Casualties are unable to fight infection, and develop severe overwhelming sepsis that is difficult to treat, even with modern intensive care. Other blood components essential for coagulation and clotting are also affected leading to uncontrolled bleeding and clot failure. Together these result in a peak of mortality between 30 and 60 days. Without treatment, 50% of individuals exposed to whole body doses of around 4 Gray will die by 60 days post exposure<sup>5</sup> (33).

Recently filgrastim (or pegfilgrastim), currently marketed under the trade names Neulasta<sup>6</sup> or Neupogen<sup>7</sup>, provide an effective means of supporting white cell progenitor cells in bone marrow following radiation exposure. They have shown in animal models, and now human models, that a single injection of Neulasta or Neupogen, delivered in an autoinjector similar to those seen to treat severe allergy, approximately doubles the average dose of radiation required to kill personnel. That is, the LD<sub>50/60</sub> increases from approximately 4 Gray to approximately 8 Gray (34-42).

The availability of Neulasta or Neupogen as an effective anti-radiation sickness MCM has significant impacts on the kinds of possible radiological exposures that might be endurable during operations, and provide assurance and support in the event of catastrophic accidental high dose exposure. Additional interventions, such as prophylactic harvesting of circulating white blood cell progenitors (stem cell donation), may also provide additional avenues of protection against accidental high dose exposures in at risk military populations. Early research in this area suggests that the addition of autologous bone marrow transplantation to Neulasta increases the LD<sub>50/60</sub> to above 10 Gray. This increase is so significant that previously unseen

<sup>5</sup> This measure of radiological toxicity is known as LD<sub>50/60</sub>

<sup>6</sup> Neulasta® is manufactured by AMGEN® (<https://www.neulasta.com/>)

<sup>7</sup> Neupogen® is manufactured by AMGEN® (<http://www.neupogen.com/>)

pathological effects of radiation exposure at around 9 Gray, masked and not clinically apparent due to mortality at lower exposure levels, are now clinically observable and amenable to investigation and treatment (32, 33).

### Implications of the CBRN hardened soldier

Technologies such as bionics, electronics, robotics, genetics, nanotechnology and wireless communications have opened new research opportunities for the development of enhancements. Most enhancements fielded until today have provided improvements in performance, generally to a predefined minimum standard of health or performance, that are reversible and do not result in permanent change to the individual. Recent technological developments now allow for researchers, decision makers and organisations to cross ill-defined boundaries between fully reversible and short term enhancement into new territory of augmentation that may have permanent or unpredictable short and long term effects on individuals. Such technologies have the potential to permanently alter, without predictable outcome, the human genetic pool (1, 2, 43, 44) without considering or account for future impacts. The two examples shown above highlight that there is impetus to move towards more intensive augmentation and enhancement of military forces, and that there has been little if any meaningful engagement with the societies that will have to accept the consequences of these efforts.

Examples of recent enhancement and augmentation research can be divided into a number of categories. Augmentation of physical capabilities – strength, mobility, protection and soldier-machine integration (local or remotely) – have been extensively explored including investigations into exoskeletons, liquid and dynamic armour. Augmentation of cognitive capabilities – awareness, attention, memory, planning, learning, language and communication – have been explored with efforts to develop real time language translation for tactical use, situation awareness augmentation and automated inference of commanders' intent during planning. Augmentation of human senses – sight, smell, hearing, touch and taste – have equally been extensively investigated including dual use technologies such as haptic feedback, electronic tongues, electronic pass through hearing protection, and telescoping contact lenses. Augmentation of human metabolism – physiological endurance, metabolism of foods, sleep requirements, and overall wellbeing – are the subject of detailed ongoing investigation with attempts to abolish the requirement for sleep, reduce dependence on regular food intake and increase stamina and endurance in high stress environments (1, 3, 43).

At the leading edge of research, civil-military cooperative research programs have investigated some military enhancement and augmentation concepts that have only until recently been conceived in fiction. These have included investigations into metabolic modification to enable suspended animation like states and hibernation, near immediate altitude and hypoxia

acclimatisation, mind-machine interface for better control of robotic prostheses following amputation or enhanced operational command control and planning, nanotherapeutics and autonomous diagnostics and therapeutics (i.e. self healing) (1, 3, 43).

Such augmentation raises serious questions, not only ethical questions but questions of leadership, legality, conduct of military operations, individual psychological impacts and trauma and intergenerational impacts. For instance, could augmented soldiers be considered “weapons” in themselves and therefore subject to regulation under Laws of Armed Conflict (LOAC) or be defined as “biological weapons” when considering the provisions of the Biological and Toxin Weapons Convention? Will augmented personnel work harmoniously with non-augmented personnel, or be a segregated and hostile subpopulation? If augmentation cannot be reversed, what are the longer-term impacts for the personnel? Will they be able to reintegrate successfully into civilian life at the end of their service life? Are military personnel – themselves in a hierarchical structure and open to coercion and bias of many types – able to give valid enough informed consent for augmentation, particularly where it might have whole of life effects, or effects in progeny across generations (such as arises from genetic modification)? What are the parameters for defining “acceptable risk” for the purpose of implementing augmentation across a military population? (1)

Some of these questions have been the subject of intense debate in philosophical and bioethical circles over the past decades. A recent report has provided a useful framework for exploring these ethical issues, and highlights that ongoing military research and development into enhancement and augmentation is generating policy vacuums that are becoming wider as technological advances continue (1). They raise concerns that enhancement and augmentation research is accelerating with technological innovation and that much of the work is occurring without sufficient ethical or legal consideration. This, they say, is generating risk uncertainties that may ultimately result in strategic surprise and negative societal outcomes (1-3, 44).

Balanced against this, however, is that near-peer military rivals are sizing up mutual war-fighter enhancement and augmentation efforts. The new opportunities emerging due to technological innovations such as augmentation and enhancement create new opportunities for great power competition and “arms races”. Western militaries may be experiencing a classical military operational and ethical dilemma – what may be ethically unpalatable may be nonetheless militarily necessary - failure to invest in enhancement and augmentation research and development may result in strategic and potentially decisive operational disadvantages with significant real-world ramifications.

There may come a point where CBRN force protection enhancement and augmentation becomes sufficiently sophisticated that many traditional CBRN agents, and the systems designed to defend against them, become

obsolete and thus neutralised as threats. Such enhancements, improving on the human body's ability to defend against exposure to an agent or recover more effectively and return to operations, are currently temporary in nature and fully reversible and there are no known long-term outcomes on the individual. Such reversible interventions are seen as more ethically acceptable, and more readily accepted by front line personnel who at the individual level generally desire the maximum level of protection possible. For a military to take the next steps and deliver both CBRN enhancement *and* augmentation technology, thorny ethical issues surrounding consent, disclosure, duress, undue influence, autonomy, beneficence and non-maleficence at the individual and population level will need to be addressed (1, 43).

The question is, where will the arms race of enhancement and augmentation end? Lin, Mehlman and Abney parallel the recent highly publicised technological advances and research to develop battlefield robots able to deal with the complexities of the modern battlespace, with intensive but less well publicised human augmentation research to develop more augmented and engineered humans able to manage a wider range of physiological and physical insults (1). They summarise this neatly, suggesting that on the one hand we are attempting to make machines more human and on the other are attempting to make humans more machine. The ethical debate surrounding the benefits and risks of this general research direction is intense and ongoing (2, 3, 44, 45). These are not new arguments – an important historical example touching on these ethical concerns being the philosophical arguments of Nietzsche in the late 19<sup>th</sup> century espousing the virtues of the “Übermensch” class (45) and the subsequent counter-arguments to Nietzsche's propositions by Santayana (46). In conclusion, accelerating technological innovation and new research methodologies are opening enhancement and augmentation possibilities previously only dreamt of, or found in fiction. Traditional ethical and moral standards are subsequently being challenged and stressed, and organisational and social policy and understanding are lagging. While enhancement offers apparently ethically acceptable solutions to high risk problems, such as CBRN force protection, future developments are likely to touch on the boundaries of acceptability and risk – a challenge in a strategic landscape where miscalculation can have significant and long term negative outcomes.

### Conflict of interests

The author has no conflicts of interests to declare.

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